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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/634,114	08/04/2003	Gary D. Glick	UM-08192	6392

7590 05/31/2006

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EXAMINER	
KIM, VICKIE Y	

ART UNIT	PAPER NUMBER
1618	

DATE MAILED: 05/31/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/634,114	GLICK, GARY D.	
	Examiner	Art Unit	
	Vickie Kim	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 6-20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 6-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *1/06;4/06;9/05;6/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election acknowledged

1. Applicants' election with traverse the invention group I of claim 1 and the Bz-423 as the elected species is acknowledged. The restriction is made without traverse. Therefore, the restriction requirement is deemed to be proper and made FINAL.

Status of Application

1. Acknowledgement is made of amendment filed 3/23/2006. Upon entering the amendment, the claims 2-5 are canceled.

New claims 6-20 are added.

2. claims 1 and 6-20 are pending and presented for the examination.

Information Disclosure Statement(IDS)

The information disclosure statement (IDS) is submitted on 1/23/2006; 4/24/2006;9/6/2005; and 6/21/2004. The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner. Please refer to applicants' copy of the 1449 submitted herewith.

Claim Rejections - 35 USC § 112, 1st

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Scope of Enablement

1. **Claims 1, 7-20** are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims because the specification, **while being enabling for making a specific benzodiazepine derivatives such as BZ-423**, does not reasonably provide enablement for all types of compounds having generic structure as recited in claim 1

Attention is directed to In re Wands, 8 USPQ 1400 (CAFC 1988) at 1404 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing Ex parte Forman, 230 USPQ 546 (BdApls) at 547 the court recited eight factors:

1) *The nature of the invention:*

The instant invention is drawn to a composition comprising a drug-eluting stent media using an effective amount of an benzodiazepine compounds such as Bz-423.

(2) *The state of the prior art*

There are numerous compounds having similar structure with different pharmacological activity due to its sensitive receptor binding activity, drug –drug, carrier or unexpected biological actions.

Furthermore, for a pharmaceutical composition containing multiple active ingredients or carriers having different chemical structures and modes of actions, their interaction, co-action, e.g. synergism etc. is even more unpredictable. The

specification does not provide any competent evidence or disclosed tests that are highly predictive for the pharmaceutical use of the instant compounds in the treatment of all the claimed conditions. It is well recognized fact in the art that isomers or enatiomers or tautomers may have different pharmacological activities and various level of receptor binding activities.

The high degree of **unpredictability** in pharmacological activity in general and the drug treatment is well known in the art. A slight change in the structure of the drug would drastically change its influence on receptor binding activity and selectivity. Note that in cases involving physiological activity such as the instant case, " the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved". See In re Fisher, 427 F 2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).

(3) *The relative skill of those in the art*

The relative skill of those in the art of pharmaceuticals is high.

(4) *The predictability or unpredictability of the art*

The specification does not provide any competent evidence or disclosed tests that are highly predictive for the pharmaceutical use of the instant compounds. Pharmacological activity in general is a very unpredictable area. Note that in cases involving physiological activity such as the instant case, "the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved". See In re Fisher, 427 F.2d 833, 839, 166

USPQ 18, 24 (CCPA 1970). Especially, Bono et al(1999, Peripheral benzodiazepine receptor agonists...) states that antiapoptotic activities are influenced by (i) a close correlation between the antiapoptotic activity of carious PBR agonists and their respective affinity for the PBR agonists and their respective affinity for the PBR determined on the same cells(ii) a lack of effect of central benzodiazepine receptor agonists such as clonazepam on cell survival (iii) the lack of an antiapoptotic activity of Ro5-4864 on wild type Hurkat cells(lacking the PBR receptor) and the reappearance of this effect on PBR-transfected Jerkat cells, and (IV) the blockade of the antiapoptotic effect of PBR agonists by a selective PBR antagonist. Thus, the regulation of cell death is unpredictable as known in the art

(5) *The breadth of the claims*

The instant claims embrace numerous Markush types compounds. If the compounds having this broad scope is obvious variant over the claimed structure because of its core structure, one would have easily conclude that all the claimed inventions(all compounds claimed) are obvious over benzodiazepines or benzodiones which are already well known in the art. If inventive concept is based on novelty of the compounds claimed, applicant intention is self-conflicting with the knowledge on pharmacology available in the art.

(6) *The amount of direction or guidance presented, and presence or absence of working examples*

Although the specification provide enabling disclosure for Bz compounds(e.g. Bz-423), none of the specification provides enabling disclosure for all the compounds as claimed.

The specification provides no guidance, in the way of enablement for the full scope of all agents as claimed. The skill artisan would have not known that which compounds of the claimed compounds are capable of accomplishing the desired result of the claimed invention without undue amount of experimentation.

The specification provides lack of evidential support substantially where any skilled artisan can not clearly understand how the claimed invention(i.e. a composition comprising a compound as claimed) is made and used at the time of the invention with the information provided and thus, the claims are considered not enabled with the information given.

(7) *Quantitation of undue experimentation.*

Since insufficient teaching and guidance have been provided in the specification, one of ordinary skill in the art, even with high degree of skill, would not be able to use the compound for all types of compounds as claimed without undue experimentation.

The true fact of the state of the art in said therapy is expressed well, "The significance of particular drug treatment for modifying different aspects of biological activity cannot be predicted a priori but must be determined from the case to case by painstaking experimental study and when the above factors are

weighed together, one of ordinary skill in the art would be burdened with undue "painstaking experimentation study " to determine the efficacy.

Double Patenting

2. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

3. Claims 1, 6-20 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims of copending Application No. 10/427212. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claimed invention from both applications is utilizes very same benzodiazepine compounds having substantially same pharma-core structure. The difference of the instant claims from the claims of US212 application is drug-eluting stent media , however, the application of benzodiazepine with

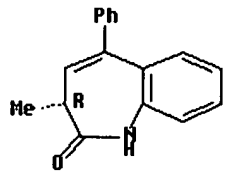
stent media is obvious because the utility of benzodiazepine is well known in the field (see US 2002025946). This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Reasons for allowance

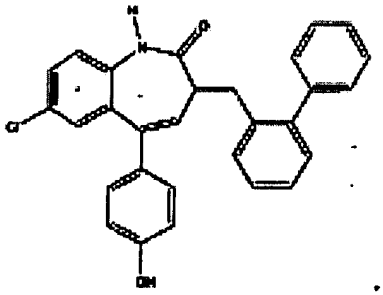
1. Claim 6 includes allowable subject matter.

2. The following is an examiner's statement of reasons for allowance:

Snyder et al(US2002/0128208) teaches N-arylbenzamides containing composition used as non-peptide agonists and antagonists of vasopressin receptors. The N-arylbenzamides taught in the patent has general structure as following:



The claimed compound has materially different substituent on R4 position which is nor taught or suggested by Snyder's patent and furthermore, the sub-generic compounds taught in the patent is considered to be patentably distinct from the species claimed in instant claims due to the different physical and chemical properties, which is exemplified with elected species having the structure as following:



The claims are considered to be novel over the prior art of the record, and thus, the a drug-eluting stent media composition which comprising said novel composition as mentioned is also considered to be novel over the prior art of the record.

3. Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

Conclusion

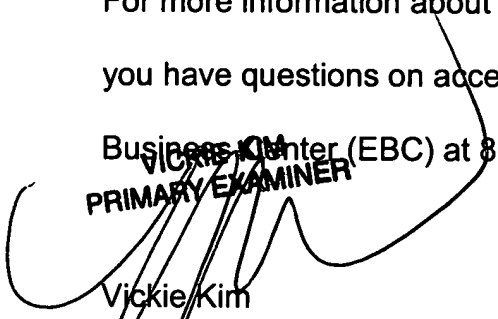
1. No claim is allowed.

2. Claim 6 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form or incorporated into claim 1 to include all of the limitations of the base claim and any intervening claims. Double Patenting rejection has to be obviated by filing Terminal disclaimer to put the claim 6 under allowable condition.

3. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Vickie Kim whose telephone number is 571-272-0579. The examiner can normally be reached on Tuesday-Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G Hartley reached on 571-272-0616. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Vickie Kim
Primary Patent Examiner
Art Unit 1618